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Assessment of dose and DNA damages in individuals exposed to low dose and low dose rate ionizing radiations during computed tomography imaging

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ABSTRACT

Purpose: Computed tomography (CT) is a frequently used imaging modality that contributes to a tenfold increase in radiation exposure to the public when compared to other medical imaging modalities. The use of radiation for therapeutic need is always rationalized on the basis of risk versus benefit thereby increasing concerns on the dose received by patients undergoing CT imaging. Therefore, it was of interest to us to investigate the effects of low dose and low dose-rate X-irradiation in patients who underwent CT imaging by recording the doses received by the eye, forehead and thyroid, and to study the levels of damages in the lymphocytes in vivo.
Materials and methods: Lithium manganese borate doped with terbium (LMB:Tb) thermo luminescence dosimeters (TLD) were used to record the doses in the patient's ($n = 27$) eye, forehead, and thyroid and compared with the dose length product (DLP) values. The in vivo DNA damages measured were compared before and after CT imaging using chromosomal aberration (CA) and micronucleus (MN) assays.
Results: The overall measured organ dose ranged between 2 ± 0.29 and 520 ± 41.63 mGy for the eye, 0.84 ± 0.29 and 210 ± 20.50 mGy for the forehead, and 1.79 ± 0.43 and 185 ± 0.70 mGy for the thyroid. The in vivo damages measured from the blood lymphocytes of the subjects showed an extremely significant ($p < 0.0001$) increase in CA frequency and significant ($p < 0.001$) increase in MN frequency after exposure, compared to before exposure.
Conclusion: The results suggest that CT imaging delivers a considerable amount of radiation dose to the eye, forehead, and thyroid, and the observed increase in the CA and MN frequencies show low dose radiation effects calling for protective regulatory measures to increase patient's safety. This study is the first attempt to indicate the trend of doses received by the patient's eye, forehead and thyroid and measured directly in contrast to earlier values obtained by extrapolation from phantoms, and to assess the in vivo low dose effects in an Indian patient population undergoing CT procedures.

1. Introduction

Diagnostic radiology contributes very importantly to the early detection of disease. However, it constitutes also an important man made source of radiation [1]. A recent study shows that a significant enhancement of imaging procedures resulted in a concomitant increase in the annual per capita effective dose from 0.54 mSv to about 3.0 mSv, of which the largest part (49%) was due to computed tomography (CT) scanning and nuclear medicine [2,3]. Mettler et al. [2] emphasized that in addition to effective dose (ED), absorbed organ doses are important, as the stochastic risks of carcinogenesis and genetic effects are quantified by the ED which is an index of detriment averaged over population types, ages, sex, from risk projection models [4]. In CT, for some procedures, the organs in the beam may receive doses of 10–100 mGy with an average of 15–30 mGy per CT scan [5–11]. Moreover,

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effective doses to a neonate for a head CT examination are evidently higher than in adult's. Thus, the effective doses of diagnostic X-ray examinations depend upon machine parameters as well as procedures. However, also the biological (genetic) constitution of the individual plays an important role in the responses to these relatively low radiation exposures. Without any doubt, diagnostic procedures provide great benefits. Nevertheless, the possible health risk of developing stochastic effects from such exposures need to be investigated. Occupational exposure is regulated in healthcare and nuclear industries. However, it is somewhat more difficult to regulate the exposures of patients because the medical benefits of diagnostic (and also radio-therapeutic) radiation mostly prevail over the long term side effects. The new trend of personalized medical exposure this is already taking into account. Several studies have reconnoitered the incidence of chromosomal aberrations (CA) and the formation of micronucleus (MN) after exposure to radiation in nuclear power plant workers [12], radiation workers [13], and hospital workers in the units of medical imaging [14], radiotherapy [15], cardiology [16], nuclear medicine [17], operating rooms [18], and in dental clinics [19] . Nonetheless, the data on biological monitoring of patients undergoing CT exposed to low doses of radiation and its relation to organ doses and effective dose are still lacking. Therefore, this investigation was designed to calculate effective dose. Organ doses to the eye, forehead, and thyroid were measured and the dose effect relationship of calculated doses to radiation induced DNA damages in blood lymphocytes determined in the same individuals.

2. Materials and methods

2.1. Study population

The study population consisted of twenty seven subjects ($n = 27$) who underwent CT imaging in the Department of Radiology, Sri Ramachandra University. The study was approved by the Institutional Ethics Committee (IEC no/13/DEC/32/241). About 3 ml of human peripheral blood was collected at two intervals, once before exposure (B.E.) and next 2–3 h after exposure (A.E.) from all twenty seven study subjects, and used to measure DNA damages.

2.2. Measurement of organ dose using lithium magnesium borate doped with terbium thermo luminescent dosimeters

The effective doses to the study subjects were obtained from the inbuilt dose length product (DLP) meter present in the CT. DLP refers to the total absorbed dose over the length of a scan. The DLP values were converted into effective doses by multiplying it with the specific organ coefficients (*K* factor). The absorbed radiation doses to the eye, forehead, and thyroid were measured using near tissue-equivalent thermo luminescence (TL) material of lithium magnesium borate doped with terbium (LMB:Tb); developed at Indira Gandhi Centre for Atomic Research (IGCAR) by the solid state diffusion technique [20]. Approximately, 50 mg of the polycrystalline powder (size below 150 μm) of LMB:Tb in sealed polythene bags (size 1 × 1 cm) (Fig. 1a) were labeled and fixed near the eye, forehead and thyroid of the subjects (Fig. 1b) undergoing the CT to record the individual's doses received by these organs. After the procedure, TL material (~10 mg) was used to measure the dose as described in detail from our laboratory [20]. For each subjects, the TL material was read three times and the average was taken as the final dose. According to the standardized protocol, published calibration factor for the TL material was calculated by exposing the TL powder using gamma rays of energy 662 keV emitted from a Cs-137 source.

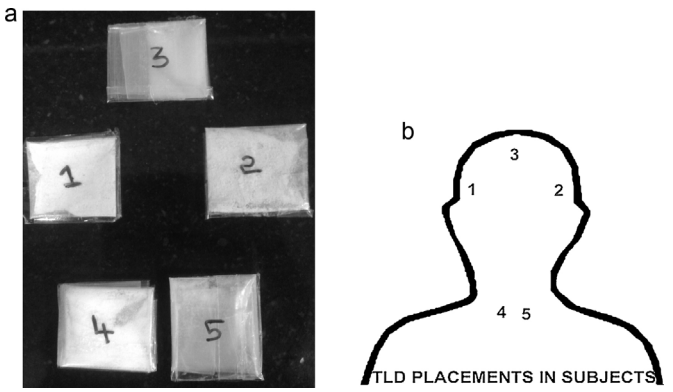

Fig. 1. (a) 50 mg of the polycrystalline thermo luminescent dosimeter (TLD) powder of lithium magnesium borate doped with terbium (LMB:Tb) in sealed polythene bags (size 1 × 1 cm). (b) Placement of sealed lithium magnesium borate doped with terbium (LMB:Tb) Thermo luminescent dosimeters (TLD) near the eye, forehead and thyroid of the subjects undergoing the CT to record the individual's absorbed doses (mGy) received by these organs.

2.3. Quantification of DNA damages

The DNA damages were measured from the blood samples using CA and MN assays. About1 ml of peripheral blood was added to 8 ml of RPMI 1640 medium (GIBCO, Grand Island, New York, USA), supplemented with 2 ml of fetal bovine serum (GIBCO, Grand Island, New York, USA), and 400 μl of PHA (GIBCO, Grand Island, New York, USA) as duplicates, and the cultures were incubated at 37°C in a 5% CO_2 atmosphere. At the 24th hour, the cells were arrested at metaphase by adding colchicine (0.02 μg/ml) (GIBCO, Grand Island, New York, USA) and further incubated for 24 h. At the end of the 48th hour of incubation, the samples were harvested with exposure to hypotonic solution (0.075 M KCl) and fixed using Carnoy's fixative. The cell pellet was dropped onto a prechilled glass slide.

To another set of cultures, Cytochalasin-B (6 μg/ml) (GIBCO, Grand Island, New York, USA) was added at the 44th hour of culture and further incubated for 24 h. At the end of 72 h of incubation, the samples were harvested and fixed, similar to the metaphase chromosome preparation. The slides were coded, stained in giemsa and mounted with DPX [21]. The slides were then observed for CA and MN among the binucleated cells under the microscope to calculate the aberration frequency and standard error. The mean frequencies of aberrations before and after the procedure were compared using the student '*t*' test.

3. Results

As CT examinations greatly contribute to the effective doses received by the public, the organ doses received by the eye, forehead, and thyroid were measured using TLD and compared with the recorded effective dose (DLP for each subject). Among the study subjects 63% were male and 37% were female, with an average age of 38.3 ± 16.7. Further, 26% of the subjects were smokers and 64% were non- smokers. The patients underwent CT examinations with and without contrast for abdomen, thorax, and brain. The contrast is radio opaque substance that improves vascularity while performing the CT scan. Of the subjects studied, 48% underwent CT examination without a contrast agent and 52% with a contrast agent.

3.1. Measured organ doses (TLD) and recorded effective doses (DLP) of individual subjects

The measured organ doses and recorded effective doses of individual patients are given in Table 1a and b. The effective doses